D3.7: Proposal for an ethical framework for human enhancement

[WP3 – Human Enhancement]

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Abstract

This report provides proposals towards, and discussions of, a general ethical framework for research on and development of human enhancement technologies (HET). Until now, in spite of the extensive discussions on human enhancement and its ethical aspects, both in academic as well as in popular circles, very few, if any, proposals for ethical guidelines to guide research, development and human enhancement technologies have been made In this deliverable we will consider both the pros and cons of the development of ethical guidelines at this time. We will start by distinguishing between general ethical guidelines and guidelines for specific types of enhancement. We will then present three options for developing ethical guidelines for human enhancement, if the choice is made to do so: self-contained general ethical guidelines, self-contained domain- or field-specific ethical guidelines, and general or field-specific guidelines incorporated into existing guidelines for medical, computer and engineering ethics. We will then discuss more specifically how research ethics committees (RECs) in the medical, computer and engineering sciences could implement guidelines for human enhancement into their existing protocols. Finally, in our annexes, we include two documents: firstly a reference document that RECs could use to inform researchers about ethical issues in human enhancement and how these could be addressed in their self-assessment, and secondly case studies that could further help in understanding what types of issues can arise in connection to HET.

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Information in this report that may influence other SIENNA tasks

Linked task	Points of relevance
Task 5.3	The code of responsible conduct for HET will require consideration of the issues identified in this deliverable.
Task 6.1	The report on adapting methods for ethical analysis of emerging technologies will require contemplation about the successes and challenges in the methodology used to write this report.
Task 6.4	The process of obtaining buy-in for the codes from EU and international institutions will need to build on the proposals in this report.

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Executive summary

This report provides proposals towards and discussions of a general ethical framework for research on and development of human enhancement technologies (HET). In spite of the extensive discussion of human enhancement and its ethical aspects in both academic and popular circles, there have been very few proposals, if any, for ethical guidelines to guide research, development and application of human enhancement technologies. In this report, we discuss the need for ethical guidelines for human enhancement and then propose various options of what such guidelines might look like and how they can be implemented in research ethics.

In the introductory section 1 the main aim of this report is described, the term "human enhancement" is defined and contrasted with therapeutic intervention, and ethical issues in human enhancement are briefly surveyed.

In section 2, we discuss the pros and cons of developing ethical guidelines for human enhancement at this point in time. We note the absence of focussed research programs on human enhancement, and the limited range of products and services. We also note that the technological conditions for success in HET research have recently improved, and that more and more research for therapeutic purposes could be re-appropriated for human enhancement. We then discuss whether the current state of research warrants the development of ethical guidelines for research in this area. We also discuss whether enough consensus is possible for ethical guidelines, given the strong moral disagreements that seem to exist in society and amongst scholars, and we discuss whether general guidelines are possible, or whether guidelines should be domain- or field-specific, in relation to specific types of enhancement R&D.

Next, in section 3, the focus is on concrete options for developing ethical guidelines. Next to the no guidelines development (at this point in their development) option, three options for guideline development are distinguished, which are not intended to be mutually exclusive. The first is the development of a stand-alone set of general guidelines for HET R&D. We propose that if this option is chosen, five types of guidelines should be considered to be included. The first set relates to the consideration of potential individual and societal benefits and harms of the proposed R&D. We argue that since human enhancement does not have the overriding individual benefits that medical therapy has, more consideration is needed of the societal impact of HET R&D in ethical assessments, including implications for equality, discriminatory practices, curtailment of rights, and misuse. The second set relates to the conditions under which clinical trials are warranted, the third to the treatment of vulnerable groups, and the fourth to types of R&D that are discouraged or forbidden. A fifth, optional, set concerns ethical guidelines for specific types of enhancement, such as physical and cognitive enhancements.

A second option for guideline development is the development of domain- or field-specific guideline documents. Domain-specific guidelines are guidelines for enhancement of specific types of abilities, such as physical, cognitive, affective and cosmetic enhancements. Field-specific guidelines are guidelines that relate to specific R&D fields or techniques, such as genomics, tissue engineering and neurotechnology. The structure of each of these documents could mirror the structure we have

suggested for general HET guidelines documents. A third and final option is not to create self-contained ethical guidelines documents for HET R&D, but to include sets of guidelines within existing ethical guideline documents for R&D in the medical, engineering and computer sciences (the three fields within which HET R&D is most likely to take place).

In section 4, we discuss how research ethics committees (RECs) could implement guidelines for human enhancement into their existing protocols. We argue that RECs covering the medical sciences, engineering science and/or computer sciences should consider including ethical guidelines pertaining to HET. In self-assessments, researchers should then be asked if their proposed R&D either has human enhancement goals, or if human enhancement could be a by-product or application of it. If so, they should then proceed to a consideration of ethical issues. Ethical guidelines to of a more general nature or of a more domain- or field-specific nature to support this consideration may be included. To what extent and how these guidelines contain specific prescriptions will depend on the particular local or national values that the REC takes as its starting point.

Finally, in our annexes, we include a reference document that RECs could use to inform researchers about ethical issues in human enhancement and how these could be addressed in their ethical self-assessment, along with case studies.

List of acronyms/abbreviations

Abbreviation	Explanation
ADHD	Attention deficit hyperactivity disorder
CIOMS	The Council for International Organizations of Medical Sciences
HET	Human Enhancement Technologies
ISAPS	International Society of Aesthetic Plastic Surgery
R&D	Research and Development
REC	Research Ethics Committee
UNODC	United Nations Office on Drugs and Crime

Table 1: List of acronyms/abbreviations

Glossary of terms

Term	Explanation
Human Enhancement	a modification aimed at improving human performance and brought about by science-based and/or technology-based interventions in or on the human body.

Table 2: Glossary of terms

1 Introduction

1.1 Purpose of this report

This report provides proposals towards and discussions of a general ethical framework for research on and development of human enhancement technologies (HET). We discuss the need for ethical guidelines for human enhancement and then propose various options of what such guidelines might look like and how they can be implemented in research ethics.

1.2 The definition of human enhancement

Human enhancement does not refer to a specific technology or application. Rather, human enhancement points to a wide field of interventions and technologies that in some way aim at improving human beings beyond what is considered normal. For instance, prosthetics may outperform natural limbs, drugs may boost cognitive capacities beyond normal range, and genetically modified humans might be immune to certain diseases.

In SIENNA, human enhancement is, accordingly, defined as "a modification aimed at improving human performance and brought about by science-based and/or technology-based interventions in or on the human body." (Jensen et al. 2019, p. 15)

This definition is accompanied by a main conceptual demarcation between *medical treatment*, i.e. established medical interventions to restore health, and *enhancement*, i.e. generally all interventions that go beyond restoring health. Enhancement then includes a sub-distinction between *therapeutic enhancement*, characterizing cases in which treatment is performed to a degree beyond normal health (making the patient 'better than well') and *non-therapeutic enhancement*, characterizing cases in which healthy persons undergo modifications with the explicit aim to improve certain characteristics or capabilities. Yet, it should be noted that these distinctions remain contested, as human enhancement technologies often do not allow for a clear-cut demarcation (see Jensen et a., 2018, p. 12-17). For example, an antidepressant, which works as a medical treatment for a person suffering from depression, might be considered a mood enhancement drug when taken by a healthy person.

Accordingly, the ethical framework provided in this report is unavoidably limited to pointing out general ethical aspects and issues that typically need to be addressed in the field of human enhancement, although not all issues will arise for all types of HET.

1.3 Ethical issues in human enhancement

When it comes to the ethical assessment of HET, one might think, at first glance, that there is nothing to worry about. After all, humans have tried to improve their capabilities throughout history. For example, using night vision goggles allows us to see in the dark, which we normally cannot do, drinking coffee allows us to stay focused and awake longer than we normally can etc. However, while night vision goggles can simply be seen as a tool, which we can lay aside again, and the enhancing effects of

coffee wear out soon enough, HET is often seen as more controversial. For instance, prosthetics replace limbs and thereby change the person physically and permanently. If such a procedure was performed on a healthy person, this would blatantly violate the Hippocratic Oath. Mood enhancing drugs may change one's personality, such that the person is, in some sense, not the same anymore. If so, who is to say which personality is authentic, the one before or the one after taking the drugs? Whose informed consent should count in case of conflicting answers from the person before and after taking the drug?

Thinking of HET as having drastic and permanent changes to our human nature has been generally criticized by bioconservatives as something unnatural or resembling "playing God". In this case would we still be humans or would HET be a step towards becoming "posthumans," e.g. cyborgs? Accordingly, a major worry about HET is that we should not take our evolution into our own hands. In stark contrast, HET has been highly welcomed by transhumanists. In their views HET open up possibilities to equip ourselves better for current and future challenges, e.g. when it comes to battling diseases or adapting better to different environments. In general, HET would allow us to leave our natural human limitations behind and evolve as a species on our own terms.

The middle ground between these two opposing views lies in proceeding with caution and closely monitoring the development and implementation of HET, for it certainly leads to significant ethical issues, which need to be acknowledged and addressed. For example, being enhanced will certainly give a person an advantage over others in competitive situations. Is such competition still fair? The long-standing debate on doping in sports speaks volumes on this particular ethical issue. Similarly, if a small number of people are enhanced, it might put pressure on others to get enhanced as well, just to keep up. This, in turn, could lead to an unwanted "HET arms race" and severely limit people's freedom to choose *not* to get enhanced. For example, students' off-label use of ADHD drugs for cognitive enhancement purposes may very well change expectations about overall student performance, thereby creating a new "normal" or baseline for passing tests. Moreover, assuming that at least certain types of HET would be rather expensive initially, only rich enough people would have access to it. This would deepen and solidify the divide between the rich and the poor even further. For further discussion of ethical issues in human enhancement, see the annex to this report, and the extensive analysis of them in (Jensen et al., 2019).

This report is structured as follows. In section 2, the need for ethical guidelines for human enhancement is discussed. It is concluded that there is, indeed, a need for such guidelines. Section 3 lists and explains briefly a selected number of approaches towards ethical guidelines for human enhancement. Section 4 develops a concise proposal on how guidelines for human enhancement may be implemented in research ethics.

2 Is there a need for ethical guidelines for human enhancement?

2.1 The absence of human enhancement R&D programs

Human enhancement has become a much-debated topic in recent decades, both in academic circles and in public discussions. Amazon.com lists as many as 113 books on the topic of human enhancement, most of them published in the last ten years. A search on Google for the terms "human enhancement" and "human augmentation" yields a total of 732.000 unique hits, and as many as for the term "transhumanism" which refers to a particular pro-enhancement viewpoint. Human enhancement has been a regular topic for articles and feature stories in journals like *Science* and *Nature*, as well as in newspapers like *The Guardian* and *New York Times*. It is also a topic that has been addressed frequently in science fiction and superhero movies and novels. Governmental and research organizations have produced various reports over the past twenty years that speculate on a future wave of human enhancement technologies that will reshape society.

In spite of all this attention to human enhancement, to the best of our knowledge, focused research programs in human enhancement do not exist, scientists that self-identify as human enhancement researchers are hard to find, companies that specialize in human enhancement are equally rare, and there are hardly any human enhancement technologies on the market (Jensen et al., 2019). This state of affairs has several reasons, first of all many types of human enhancement are beyond the current realm of technological possibility. Research on cognitive, moral and longevity enhancement, for example, is currently still in its infancy, and would require major breakthroughs to enable successful solutions.

A second, perhaps more defining reason for the lack of human enhancement R&D is that approval for it is difficult to obtain. Regulatory frameworks are geared towards the development of treatments (Jensen et al., 2019). Approval for products is difficult to obtain, approval for clinical trials is not likely given without the promise of clear therapeutic benefits. In addition, medical scientists and practitioners may be hesitant to develop or apply human enhancement technologies because these may be seen to violate the Hippocratic Oath or the Declaration of Geneva, which seem to prescribe that any risk of harm to patients can only be taken in the interest of therapy. Some types of human enhancement research, moreover, are severely restricted because of existing regulations targeted at them. This holds, in particular, for physical enhancement for performance, which is heavily regulated because of its potential use in professional sports, and for germ-line enhancement, which is outlawed or severely restricted in many countries.

2.2 Arguments for and against ethical guidelines

If little human enhancement research currently exists, and future research is likely to be limited by current regulations and institutional requirements, is it, nonetheless, necessary to put ethical

guidelines in place for human enhancement R&D? One could argue that because there hardly is an existing or emerging field of human enhancement research, it is premature to do so at this point.

On the other hand, there are also reasons to believe that in spite of the aforementioned obstacles to the development of human enhancement as a field, more and more human enhancement R&D will take place in the coming years. A first reason for this is that recent years have seen rapid developments in many areas of biomedical engineering, including prosthetics, tissue engineering, genome editing, neurotechnology and nanomedicine, that could conceivably be used for enhancement purposes, even though they are being developed for therapeutic uses. Because the boundary between therapy and enhancement is not clear to begin with, some of this research could easily be used for therapeutic enhancements which, if proven to be safe and effective, could lead to subsequent non-therapeutic enhancements. In these cases, funding will initially have been granted to R&D for new therapies, and clinical trials will have been conducted for therapeutic applications, but the enhancement applications will be so similar to the therapeutic applications that they can be attained with little additional funding and testing.

In addition, because most types of human enhancement research are not prohibited, R&D with a specific focus on enhancement is still likely to proceed as well, especially when there is a promise for a market for it. There will be scientists who pursue human enhancement research out of intellectual curiosity and personal interest, and companies will emerge that produce enhancement products for which they expect popular demand. Some of the R&D that will take place will be done in countries with lax requirements for clinical trials. Some of it will take place in regulatory grey zones or vacuums, as is currently the case for the performance-enhancing drugs and nootropics (cognitive enhancers), which have seen heavy investments by private companies as well as great demand. In addition, it is already the case that defence departments in several countries have R&D programs for military human enhancement.

Therefore, even though there are few focused human enhancement R&D programs, and there are significant obstacles for such programs to exist, there are reasons to believe, in spite of the current hindrances, that the volume of human enhancement R&D and applications will increase in the future. Given this expectation, there is a reasonable justification for developing ethical guidelines now, while much of this research is still in its early stages. This calls for taking a proactive rather than reactive stance.

Another argument against ethical guidelines is that people are deeply divided over the moral permissibility of human enhancement, and that in the absence of moral agreement, ethical guidelines will be hard to forge. The moral divide is visible in the ethics literature on human enhancement, which often pits pro-enhancement transhumanists against bioconservatives. It is also visible in surveys of the general public. In a 2020 SIENNA survey among 11,000 people worldwide, we found that people are split on many moral positions regarding human enhancement. (Prudhomme et al. ,2019). However, the process of guideline development can be used to reach moral agreement between diverse stakeholders. This is how the process has worked previously for other morally contentious topics like genome editing and organ donation, but nevertheless procedures and guidelines have been established. Also, the point of ethical guidelines is not always to prescribe specific do's and don'ts.

They could also simply be an invitation to moral reflection or stakeholder engagement concerning morally controversial topics.

2.3 General or specific guidelines?

Another argument against the development of ethical guidelines for human enhancement is that the field, to the extent that there is one, is so diverse that there is not enough of a common denominator between the different practices to be usefully subjected to ethical guidelines. "Human enhancement", the argument goes, is an umbrella term for practices and applications that have little in common, ranging from eyebrow lifts to memory-enhancing drugs to germ-line genetic engineering. There are no general ethical guidelines that can usefully apply to this diversity, and each of these practices and applications require their own independent ethical analysis.

We could however argue that enhancement is in many ways the mirror image of therapy, and that we also have general ethical guidelines for therapeutic intervention, even though therapies can be very different, and even though therapies may require their own ethical considerations. There are general ethical guidelines for medical treatment, research with human participants, clinical trials, use of human cells and tissues, etc. There are widely accepted ethical guidelines that cover part or all of medical research and practice, such as the Declaration of Helsinki, the WHO Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants, the Oviedo Convention, and the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects.

Still, it is possible that general guidelines are more difficult to establish for human enhancement than for therapy, or that the ones that can be found are so general that they provide little guidance for concrete practices and applications. Possibly, a more beneficial approach could be to develop specific ethical guidelines for specific types of human enhancement R&D and applications. For instance, different sets of ethical guidelines might be developed for the six types of human enhancements distinguished in Jensen et al. (2019): cognitive, affective, moral, physical, cosmetic and longevity. Alternatively, ethical guidelines might be developed for different fields in which human enhancement R&D is performed, including, amongst others, prosthetics, genomics, pharmaceutics, neurotechnology, tissue engineering, human-machine interaction, and nanomedicine.

In the next section, we will further investigate the value of both general and domain- or field-specific ethical guidelines for human enhancement. We will do so by considering earlier proposals for ethical guidelines, through an assessment of the current state of the art of human enhancement R&D in different fields and domains, and by considering the stated needs for rules and guidelines by stakeholders.

3 Approaches towards ethical guidance for human enhancement

Aside from simply doing nothing in terms of developing ethical guidelines, three—not necessarily mutually exclusive—options of how to approach the task can be distinguished.

3.1 Option 1: general ethical guidelines for HET

This option will be more or less similar to other medical conventions and declarations, like the Declaration of Helsinki or CIOMS guidelines. The advantage of such an approach would be to have one clear point of reference and basis on which ethical assessment of HET could be conducted. Assuming that there would be a wide agreement amongst stakeholders on such general ethical guidelines, it would spare everyone the complexities and likely inconsistencies of a variety of different ethical guidelines, specific only to certain HET technologies or applications.

The downside of such an approach would be, however, that the general guidelines would likely fail to be applicable in sufficient clarity and precision to the vast variety of HET that might be developed. At least, it would require a substantial amount of interpretation in order to assess the specifics of each HET in terms of the general ethical guidelines. However, once more detailed explanations are given for certain types of HET, this could essentially amount to giving up the core idea of this approach, i.e. of having *only* general ethical guidelines.

Still, developing general ethical guidelines would certainly provide a much-needed basis for further and more specific guidelines for certain types of HET. Observing the general ethical guidelines would ensure overall consistency when dealing with the ethics of HET.

Our review of existing codes and guidelines for human enhancement has made it clear that general guidelines for HET hardly exist (Tamborino, Lanzerath et al. 2018; see also Ruggiu 2018). Nevertheless, what might such general guidelines look like? First, a distinction may be made between guidelines that concern R&D in HET and those that concern the application of HET. These could be part of the same document, but they might also be contained in different documents, the R&D guidelines being for researchers and developers, and the application guidelines for hospitals, clinics and points of sale that might equip or provide people with HET. We will focus on R&D guidelines in the remainder of this section.

A first guideline, or set of guidelines, could pertain to the justification of the R&D in terms of its benefits to individuals and society. Since human enhancement research is morally controversial and could lead to trials applications that cause harm to humans, its potential benefits should be well-established before R&D is to proceed. Medical research ethics guidelines often make a requirement of societal value, or of beneficence and nonmaleficence, and for HET research, similar requirements could be made. Dictated by these guidelines, it could be a requirement that an extensive assessment is made of potential and likely benefits as well as harms, so as to come to an overall assessment of the expected benefits to individuals and to society. This assessment would be different for R&D that is intended for therapeutic applications but could also be used for enhancement; here, the benefits and risks of both would have to be assessed together. Guidelines could include a requirement to do an extensive social and ethical impact assessment as well as to involve stakeholders in the assessment.

While for R&D for therapy, the benefits to individuals usually outweigh harm to society, this is less obviously the case for HET R&D. Therefore, assessments of benefits and risks for HET R&D should have a greater consideration of consequences for society than regular R&D in medicine. In particular, HET

applications could lead to inequality, could unfairly disadvantage certain groups (including the unenhanced), could undermine rights, could lead to new societal pressures to enhance (e.g., in the workplace, or in schools) and could lead to different kinds of misuse that need to be assessed prior to introduction to market.

Secondly, guidelines would have to be in place for the conditions under which clinical trials should proceed. Since HET research is not intended for therapeutic purposes, clinical trials will be much more controversial, and the threshold they should meet is likely to be much higher than for clinical trials for R&D for therapy. The relevant guidelines here would therefore propose a different way of balancing harms and benefits that would specifically relate to HET. An exception may be made for research that could be used for both therapy and enhancement; given that its main purpose is therapeutic in nature, such research would likely be able to be done under normal guidelines for clinical trials. Yet, the wider the scope or the higher the possible impact of the potential enhancement involved, the more specific ethical guidelines for HET would need to be used. For instance, adapted informed consent guidelines would be needed that take into account the special conditions presented by HET research.

Third, guidelines would likely be set up in relation to vulnerable groups and individuals, including children, persons unable to give informed consent, people with diseases or disabilities, the elderly, and others. This would concern both their participation in clinical trials and the possible use of HET by these groups after R&D has been completed.

Fourth, guidelines would likely be included that pertain to types of R&D that are discouraged or forbidden. Depending on the moral considerations brought to bear, there might be guidelines against human enhancement that involves germ-line engineering, paediatric enhancement, enhancement of people without an ability to provide informed consent, enhancements that grant powers and capabilities that are considered socially undesirable, enhancements that harm autonomous decision-making, enhancements that strongly alter personality traits, enhancements that severely harm bodily integrity, enhancements that are thought to be incompatible with human dignity, certain types of irreversible enhancements, enhancements that make use of scarce biological or chemical resources also used for therapy, and so on.

Fifth, and optionally, the document could provide detailed ethical guidance for specific types of enhancement. This is an optional requirement, because such guidelines could also be included in separate sets of guidelines for particular fields or topics. It could be included, first of all, for the different types of enhancement distinguished in the appended reference document: physical, cognitive, affective & emotion, moral and longevity. Secondly, they could also relate to particular fields in which enhancement could be developed, such as prosthetics, pharmaceutics, and tissue engineering.

3.2 Option 2: domain- or field-specific guidelines for HET

In this option, the focus is not on general guidelines but instead on guidelines specific for only certain types of HET. The advantage of this option would be that the specific ethical issues could be derived directly from the details of the domain or field in question. This way, the interpretive work mentioned

as a disadvantage in option 1 would be transformed into an advantage because it would be built in right from the start. Moreover, it could be ensured that the ethical assessment is sufficiently empirically informed based on domain- or field-specific-knowledge. Accordingly, the domain- and field-specific approaches should be distinguished, even though they are not mutually exclusive. The structure of each of these documents could mirror the proposed structure of general ethical guidelines for HET, but then restricted to the domain or field in question.

3.2.1. Option 2a, domain-specific approach

Specific guidelines could be developed for each enhanced human function. This could lead to different domain-specific guidelines for *physical, cognitive, affective & emotive, cosmetic, moral, and longevity* enhancements. It should be mentioned that we still include creativity enhancement in the cognitive domain, despite recent claims that it should be considered a domain in its own right (see, for instance, Hertenstein et al. 2019). Moreover, within each domain, further distinctions could be made in order to make the ethical guidelines as specific as possible for various types of HET in question, e.g. for physical enhancements of vision vs. arm strength or for cognitive enhancements of memory vs. concentration.

3.2.2. Option 2b, field-specific approach

Specific guidelines could be developed for each scientific field. This would include, for instance, *genomics, tissue engineering, neurotechnology, pharmaceutics, nanomedicine, and human-machine interaction*. Likewise, further sub-distinctions could be made in order to ensure as much specificity as possible for the scientific (sub-)field in question.

The main disadvantage of such specific approaches would obviously mirror the core advantage of general ethical guidelines. While each specific ethical guideline would be precisely empirically informed about its (sub-)domain or (sub-)field and would, therefore, be able to draw out and address the specific ethical issues in great detail, the approach would lead to vast number of very likely divergent ethical guidelines, most authors of which would probably not even aware of other specific guidelines. Hence, it would in all likelihood lead to a highly inconsistent ethical assessment of different types of HET, although at least some of them would likely be similar enough to be assessed under the same ethical point of view. This holds all the more, assuming that the same type of HET might be subsumed to different domains and fields, like in dual-use cases or in therapeutic enhancement more generally. This would make it unclear which specific ethical guideline should take precedence and be used in the first place.

Developing a shared basis for each specific ethical guideline would, of course, remedy these problems. However, this would, once again, mean giving up the very core of this option and would basically lead back to incorporating the first option, i.e. developing—at least also—general ethical guidelines for HET.

The current state-of-affairs is that for some of these domains and fields, ethical guidelines or codes of conduct have been developed, but only to a very limited extent (Tamborino, Lanzerath et al, 2018). For cosmetic surgery, to start, various codes of conduct exist, including the ISAPS Code of Ethics & By-Laws of the International Society of Aesthetic Plastic Surgery (See https://www.isaps.org/medical-

professionals/code-of-ethics/). A code of ethics relates, however, to individual professional conduct in an already established field. It is different from a set of ethical guidelines for R&D or application in that it focuses on standards for conduct rather than the content of practices, and is therefore less likely to address in detail the ethical considerations that these practices are subject to. The ISAPS Code contains general principles such as serving humanity, upholding the dignity of persons, serve the best interest of the patient, and not to operate on minors for purely cosmetic reasons. It does not address ethical issues in R&D, nor does it address the moral considerations by which one could come to a decision whether a particular cosmetic surgery is morally justified.

Ethical guidelines for performance-enhancing drugs ("doping") exist, but these are almost exclusively directed at their use in sports, and towards athletes and athlete support-staff (including medical professionals). There is little attention towards the development of these drugs. In any case, doping is only discussed in a negative way, as a form of enhancement that should not be practiced. Similarly, a United Nations report with policy recommendations regarding the non-medical use of prescription drugs (UNODC) assumes that all these non-medical uses are harmful, even as it mentions uses for enhancement, and categorizes them as instances of substance abuse that should be combated (UNODC, 2011).

3.3 Option 3: Added clauses on HET in medical ethics/research ethics documents

This option would drop the idea of having stand-alone ethical guidelines for HET. Rather, HET-specific ethical guidelines would be added to existing (medical) (research) ethics guideline documents. This approach could, therefore, take its starting point in already existing general guidelines or domain- or field specific guidelines. For example, a section on HET could be added to ethical guidelines for genomics. This option is only available if HET is not banned in the existing ethical guidelines to begin with. For instance, the Convention of Oviedo, Article 13, explicitly states that: "An intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants."

The advantages of this approach would be its efficiency and its close connection to already existing ethical guidelines. This would also ensure consistency with these existing ethical guidelines, as the HET-specific additions would be developed based on their "parent" document.

The disadvantages of this approach would more or less mirror the disadvantages of the second option. Given the vast number of specific "parent" documents, HET would likely be subject to inconsistent ethical assessments, depending on the specific ethical guideline used as "parent" document. Moreover, it would likewise lead to problems in assigning a certain type of HET to one specific existing ethical guideline to begin with, especially considering that a certain type of HET may very well be applicable in different domains and fields. Also, this approach neglects the possibility that HET raises ethical issues that are altogether novel and don't fit in with existing ethical guidelines.

3.4 General Discussion of the three options

In sum, all three approaches have their advantages and disadvantages. Yet, given that they are not mutually exclusive, the natural solution would be to opt for a combined approach. Such an approach would, firstly, consist of the development of general guidelines for HET to serve as a shared basis on how to address ethical issues in HET in general. Moreover, it would ensure overall consistency or at least provide a clear point of reference in case of complications in specific cases. Secondly, specific ethical guidelines for specific domains, fields, technologies, or applications can be developed as need be. Their development would then always take the general ethical guidelines as starting point in combination with specific (empirical) knowledge of the domain, field, etc. in question.

This is why, in the following section, we develop an idea of how to frame general ethical guidelines for HET to be used as point of reference for future, more specific ethical guidelines.

4 Implementing guidelines for human enhancement guidelines in research ethics

This section is intended to provide a framework on how ethical issues with HET may be incorporated in more specific guidelines, based on an ethical consideration of HET in general. For a general background of ethical issues in HET, which informs this framework (Jensen et al. 2019, Jensen et al. 2018 see also the reference document in the annex).

Following the advocated combination of the three options explained in section 3 above, the general ethics of HET (option 1) may lead to the inclusion of suitable questions in already existing domain- or field-specific ethical guidelines (option 3) or to the development of independent HET-specific ethical guidelines for concrete purposes (option 2).

Given that issues of human enhancement may appear in a wide variety of fields, not the least in prosthetics, genomics, pharmaceutics, neurotechnology, tissue engineering, human-machine interaction, or nanomedicine, the inclusion of suitable HET-related questions is important for respective research ethics committees (RECs). For instance, medical RECs should include the ethics of human enhancement because of possible therapeutic enhancements as well as possible non-therapeutic applications or misuse when it comes to medical research. RECs in computer science or in engineering should include suitable HET-related questions because of a likely occurrence of human enhancement in the area of human-computer interaction or bioengineering. Likewise, RECs in other fields should closely consider the possibility of human enhancement in their respective fields and add respective questions and aspects to their specific ethical guidelines.

Yet, depending on local traditions and values, how to include best the ethics of HET in detail in specific ethical guidelines will likely vary. For instance, in highly individualized societies with an emphasis on individual responsibility, the value of solidarity may not need to be accounted for to a high degree. Conversely, a society which holds solidarity in high regard would lead to higher emphasis of this value. Moreover, the value of fairness might be defined quite differently in these two societies, which would lead to differences in its inclusion in specific ethical guidelines. Finally, local traditions and values might lead to banning any HET in the first place, so that any HET-related questions in specific ethical

guidelines would simply check if human enhancement occurs or might occur and then reject the proposed R&D or treatment in question.

Consequently, we propose to allow for a variety of options when it comes to including the ethics of HET in specific ethical guidelines and REC work:

1. HET or possible HET-related applications may be banned outright. HET-related questions would then only be intended to check for the possibility of human enhancement and, should it occur, reject the proposed R&D or treatment on these grounds. This includes, of course, banning any research project with human enhancement as its specific goal.
2. HET or possible HET-related applications may be allowed under certain conditions. These conditions would mostly be informed by local traditions and values, which would already be reflected in specific ethical guidelines but would need to be complemented by HET-related questions and assessments. Any proposed R&D project or treatment would then be assessed based on these specific criteria and would only be allowed if the conditions are met.
3. No clear-cut recommendation on allowing or rejecting proposed R&D projects or treatments is made based on the ethics of HET. Instead, HET-related questions are intended to stimulate respective ethical reflection in order to make sure that possible ethical issues are sufficiently addressed. Yet, HET-related aspects would not be decisive in the RECs decision-making.

However, despite this variety of options, our general proposal is to take one of these options and include the ethics of HET accordingly in specific ethical guidelines and the considerations of REC. The starting point for both self-assessment and REC evaluation would be the following three questions:

- Is human enhancement one of the explicitly intended results of the R&D or treatment in question?
- Is human enhancement a likely side-effect or possible application of the R&D or treatment in question?
- Is it likely that the R&D or treatment in question leads to further innovations that could be used for human enhancement?

If the answer to any of these questions is yes, then the ethics of HET would need to be incorporated in the self-assessment and REC evaluation, following either of the three options mentioned above, and outlined in more detail in section 3.

First of all, harms and benefits need to be considered in all cases. R&D aiming specifically at human enhancement, including corresponding clinical trials, would need to be justified on the grounds of providing more (expected) benefits to the individual in question and society in general than harm. If at least the potential of such benefits is not well-established, the respective R&D on HET should be rejected. For cases of therapeutic enhancement or when only a possible application of the project or treatment can be used for enhancement (including corresponding clinical trials), the balancing of harms and benefits can be very complex. Also, because the benefits and harms of the non-HET part of

the project of treatment have to be considered as well. Yet, any HET-related part should then be incorporated in an overall weighing of harms and benefits, both to individuals in questions and to society in general.

Secondly, given that human enhancement is a highly diverse field, covering not only different categories of enhancement, such as physical, cognitive, affective, and others, but also different domains of application, such as healthcare, education, workplace, military, among others (Jensen et al., 2018; Jensen et al. 2019 and the reference document in the annex) it is hard to give more of a one-size-fits-all recommendation for how to include the ethics of HET in more detail, for instance how to frame specific questions or which ethical issues to include. This work of applying the ethics of HET to a concrete domain or field inevitably needs to be done by the REC in question based on local ethical traditions and values, on the one hand, and the general ethics of HET, as described especially in Jensen et al. (2019), D3.4, on the other hand.

In the reference document in the annex, we provide an exemplary indication of ethical issues and how to address them in relation to a number of important societal values, such as autonomy, dignity, fairness, among others. Depending on the importance of these values in local tradition, we suggest using them as general points of reference for the formulation and elaboration of more specific questions applicable to the domain or field in question. Of course, more societal values may be included depended on local traditions. However, it should be stressed that each additional value would need to be carefully reflected on and justified itself in terms of more general, crucial moral values, most importantly human dignity and equality.

Additionally, further specificities of the domain or field in question need to be incorporated. For example, because of the recognized autonomy of the human body, in medical treatment we are required to first obtain informed consent. This is valid also in cases that include potential therapeutic enhancement with its ethical issues. In these cases, it makes a difference whether the patient in question is an adult, capable of giving such consent, a child or a person with limited mental capacities, both of which are incapable of giving informed consent. Consequently, special attention needs to be given to the cases where vulnerable groups are involved or affected. Another special case is germ line editing for the purpose of human enhancement, where both the individual directly affected and all the following generations that are altered as a consequence of this are unable to give informed consent. Further, obtaining informed consent from an adult prior to plastic surgery involving a prosthetic is no different from the usual procedure. Yet, these types of interventions could lead to questioning whether the prosthetic includes functionalities that would enhance the patient beyond what is considered normal for them. If so, we should evaluate how this could be taken into account in the ethical evaluation of the procedure.

Accordingly, a generic suggestion for the procedure of using important societal values as starting point for formulating more precise questions and considerations in specific ethical guidelines and REC decision-making could look like this:

- In what way, if at all, would the R&D, treatment or intervention proposed affect societal value X?

- How can societal value X be safeguarded against negative effects of the R&D, treatment or intervention proposed? Could this be ensured within the proposed project or would external measures be required?
    - What specific measures are taken within the project to safeguard societal value X?
    - What external measures are proposed to safeguard societal value X?

REC evaluations would then need to consider carefully how plausible, feasible, and effective the suggested measures are for safeguarding the societal values affected. Moreover, it would need to be considered whether the answers are exhaustive, i.e. if no potential HET-related ethical issue in relation to one of the societal values has been overlooked. These considerations are, of course, not much different from the usual procedures and ethical considerations. They would just cover the added content of HET-related ethical questions and issues.

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6 Annex 1: Ethics reference document

6.1 Introduction

Human enhancement does not refer to a specific technology or application. Rather, human enhancement points to a wide field of interventions and technologies that in some way aim at improving human beings beyond what is considered normal. Consider, for instance, prosthetics that can outperform our natural limbs; drugs that can boost our cognitive capacities beyond our normal range; or genetic modification that would allow us to be immune to certain diseases. Human enhancement can, thus, be defined as a modification aimed at improving human performance beyond normal functioning and brought about by science-based and/or technology-based interventions in or on the human body.

Aside from interventions explicitly aimed at enhancement and performed on normal abled persons, enhancement may be a byproduct of medical treatment in case the treatment allows for making the patient *better than well*. *Medical treatment* typically covers established medical interventions to restore health. Enhancement would then cover all interventions that go beyond restoring health. However, no clear line can be drawn between treatment and enhancement with regard to the type of intervention. For example, an antidepressant, which works as a treatment for a person suffering from depression, might be considered a mood enhancement drug when taken by a healthy person. *Therapeutic enhancement* covers cases in which treatment of unhealthy persons is performed to a degree beyond normal health; whereas *non-therapeutic enhancement* covers cases in which healthy persons undergo modifications with the explicit aim to improve certain of their characteristics or capabilities. Accordingly, the issue of human enhancement may appear in a wide variety of fields, not the least in prosthetics, genomics, pharmaceutics, neurotechnology, tissue engineering, human-machine interaction, or nanomedicine.

In the following, we use the abbreviation **HET** for human enhancement technologies.

At first glance, HET may seem uncontroversial. After all, humans have tried to improve their capabilities throughout history. For example, using night vision goggles allows us to see in the dark, which we normally cannot, drinking coffee allows us to stay focused and awake longer than we normally can.

However, while night vision goggles can simply be seen as a tool, which we can lay aside again, and the enhancing effects of coffee wear out soon enough, HET is often seen as more controversial. For instance, prosthetics replace limbs and thereby change the person physically and permanently. If such a procedure were performed on a healthy person, this would blatantly violate the Hippocratic Oath. Mood enhancing drugs or deep brain stimulation may change one's personality, such that the person is, in some sense, not the same anymore. If so, who is to say which personality is authentic, the one before or the one after taking the drugs? Whose informed consent should count in case of conflicting answers from the person before and after taking the drug?

When thinking of HET resulting in such drastic and permanent changes of our very human nature, it has generally been criticized as something unnatural or akin to "playing God." Would we even still be humans anymore or would HET be a step towards becoming "posthumans," e.g. cyborgs? Accordingly, a major worry is that we should not take our evolution into our own hands.

Still, even if HET were not rejected outright but allowed when closely monitored, it leads to significant ethical worries, which need to be acknowledged and addressed. For example, being enhanced will certainly give a person an advantage over others in competitive situations. Yet, is such a competition still fair? Just think of the whole debate on doping in sports.

A closely related worry is that once a small number of persons are enhanced, this puts pressure on anyone else to get enhanced as well in order to keep up. This could lead to an unwanted "HET arms race" and severely limit people's freedom to choose *not* to get enhanced.

Moreover, assuming that HET is rather expensive at least initially, only rich enough people might have access to it. This would obviously deepen and solidify the divide between the rich and the poor even further.

6.2 Categories

In order to map the HET terrain, we divide HET into the following six categories:

1. **Physical** enhancements are interventions that improve or introduce new physical abilities. Potential targets for physical enhancement are performance, endurance, or the addition of new abilities (additive). Performance enhancements increase the capacity to effectively complete physically demanding tasks, like running quickly or lifting heavy objects. Endurance enhancements increase the capacity to engage in physically demanding tasks for extended periods of time. In some cases, performance and endurance enhancements will overlap; i.e., a single intervention may increase performance in such a way that it also improves endurance, or vice-versa. Additive enhancements add new physical abilities that an individual could not have without the enhancement; i.e. adding novel abilities, like seeing clearly in the dark.
2. **Cognitive** enhancements are interventions that improve cognitive abilities. Potential targets for cognitive enhancement are intelligence, clarity and creativity (although it might be argued that creativity enhancements constitute their own domain; see, for instance, Hertenstein et al. 2019). Intelligence enhancements improve capabilities associated with intellectual abilities, such as critical thinking, reasoning, memory or comprehension of ideas. Clarity enhancements are primarily related to focus but can also apply to enhancements that increase abilities associated with maintaining rigor during cognitive tasks. Creativity enhancements improve inventiveness, artistic ability, design-related tasks, or, more broadly, the ability to think of new ideas or concepts. Finally, the distinction between cognitive and physical enhancements may not always be clear, for instance in the case of sensory enhancement, which includes a physical and cognitive dimension.
3. **Affective & emotion** enhancements are interventions that improve and/or provide greater control over a human's affect and/or emotion. Potential targets for affective and emotion enhancement are mood, emotion and possibly empathy. Mood enhancements give a user control over their mood, such as by allowing a user to quickly, perhaps (in the future) even instantaneously, transition from feeling anxious about work while at home to feeling more

comfortable. Emotional enhancements alter the user's emotional state, for example by making a user feel happy quickly, or perhaps (in the future) even instantaneously, after taking a pill.

4. **Cosmetic** enhancements are interventions that improve the cosmetic traits of a human being. There are two subcategories of cosmetic enhancement: aesthetic and body modification. Aesthetic enhancements improve one's physical features to better accord with social ideals, such as cosmetic plastic surgery. Body modification entails augmenting oneself by introducing new (primarily) cosmetic features, such as 'installing' magnetic fingertips. Cosmetic enhancements share a grey area with physical enhancements.
5. **Moral** enhancements are interventions that modulate or foster attitudes and behaviors that are considered moral or socially acceptable. Potential targets for moral enhancement range from limited enhancements, for example interventions designed to 'correct' behaviors considered deviant in one's society, to more robust interventions that greatly alter or allow for the modulation of moral deliberation.
6. **Longevity** enhancements are interventions that extend a human's expected lifetime or make someone less frail and more able than normal for their age. Longevity enhancements may be preventative or may improve one's senescence or durability. Preventative enhancements stop or reduce negative effects of disease or disability, such as a vaccine. Senescent enhancements stop or slow down the aging process of the body. Durability enhancements improve one's ability to survive or recover from harm or damage.

6.3 Domains

In order to map the HET terrain further, HET could be applied in the following domains, which can be used to demarcate HET applications:

1. **Healthcare**: This domain comprises mainly institutional healthcare, including the relation between and amongst medical personnel and patients, and is mostly concerned with therapeutic enhancement.
2. **Education**: This domain comprises all stages of mainly institutional education, ranging from preschool to university and including the relations between the people involved in the education system. It also includes the effects on society in general.
3. **Workplace**: This domain covers situations at work, including the relation between employers and employees, as well as the effects on society in general.
4. **Military/defense**: This domain comprises military/defense institutions and their personnel as well as the likely impact of HET on the understanding and practice of future armed conflicts.
5. **Home or recreation**: This domain covers the use of HET purely for private or recreational purposes, including possible off-label use, and its impact on society in general.

6.4 Societal values

The following societal values are often affected by HET and raise ethical issues:

- **Autonomy**: The value of a person's ability to decide and act on her own authentic desires and preferences, without being unduly influenced, coerced or manipulated by others. HET may affect this value in either undermining or questioning but also promoting autonomy. For instance, consider again the case of mood enhancement drugs. If the person is, in some sense,

no longer the same, which would be the person's *authentic* desires and interests, based on which we would consider a decision autonomous? Furthermore, consider the possibility of a "HET arms race" due to social pressure. People would then no longer be truly autonomous in deciding for or against using HET.

- **Dignity**: The inherent, equal, and unalienable value of persons/human beings as such. HET may affect this value in that the social pressure to enhance may create a "new normal," which could lead to seeing every non-enhanced person as inferior. Consider, for instance, the fact that nowadays it is normal in modern societies (i.e. it is the norm) to own a smartphone (a trivial non-HET example), while around 15 years ago this was clearly the exception. Accordingly, imagine the different replies to someone who said s/he does not have a smartphone. While not owning a smartphone may admittedly have only little effect on respecting the person's dignity—hence the triviality of the example—not being enhanced may in the future have a significantly more serious impact on how the person is seen and treated.
- **Equality**: The value of treating everyone as equal and demanding convincing reasons for unequal treatment. Like with (equal) dignity, HET may affect equality in that it creates a whole new dimension of inequality among people. Enhanced and non-enhanced persons may very well no longer be treated *as equals*. Moreover, even if they are, enhanced persons may have unequal, namely better, chances in competitive situations. Accordingly, may HET serve as a convincing reason for unequal treatment or rather establish a requirement of again unequal, now compensatory, action toward non-enhanced persons?
- **Fairness**: The value of treating everyone in a manner that can be justified to everyone affected instead of treating people on arbitrary grounds. Like equality, HET may affect the value of fairness. Consider again the case of doping in sports. Would a competition between enhanced and non-enhanced persons still be fair? Would HET constitute a convincing or rather arbitrary criterion for treating enhanced and non-enhanced persons differently? And could such a difference in treatment be, in turn, considered fair?
- **Health & safety**: The value of both the fact of being in good health and in a safe environment as well as one's individual feeling or impression of being healthy and safe. As science-based and/or technology-based interventions in or on the human body, HET unavoidably includes risks for both health and safety. Such risks need to be carefully weighed against the expected benefits. Hence, a good case has to be made for why HET interventions warrant taking the risks involved.
- **Peace**: The value of living in a society with no or only very little violence and armed conflicts and in which conflicts are settled according to defined and accepted social rules. Although it might seem a little far-fetched at first glance, current and future developments of HET, especially possible military applications, may seriously affect the value of peace. Consider an enhanced military, which would apparently lower the risks of failure in combat. Arguably, this might lead to considering military options quicker than before or other nations being tempted to act pre-emptively. In any case, HET might lead to a quite literal "HET arms race."

- **Privacy**: The value of being in sufficient control over decisions in one's personal life and one's personal information, i.e. over who has access to this information. HET may affect this value based on a suitable enhancement technology involved. Consider prosthetics including human-robot interaction. Such a technology might very well create certain personal data, like location or usage data, which then might be accessed without the enhanced person's consent and used for a variety of questionable purposes.
- **Respect for human life**: The value of our practice of holding human life dear and in accordance with human dignity. As with the value of dignity, HET may affect seeing enhanced and non-enhanced persons differently, with non-enhanced persons being seen only as second-class citizens, who, for instance, may no longer have equal access to health care. The corresponding devaluing general attitude could be that it is these persons' own fault; they could and should have enhanced themselves. Furthermore, consider enhancements on a genetic level, which might very well include and encourage an attitude of seeing only enhanced life as worth living. This might lead to a form of eugenics.
- **Solidarity**: The value of our practice of communal and social support in which more powerful persons or groups share their resources to support less advantaged persons or groups. Like with equality and fairness, HET may affect solidarity due to a distinction between enhanced and non-enhanced persons. Who is to say that enhanced persons still show solidarity with non-enhanced persons, especially if the latter are considered to be responsible for their shortcomings? HET may, thus, encourage a new social divide between *us* (enhanced persons) and *them* (non-enhanced persons).

6.5 How to address ethical issues of human enhancement

Assuming that HET should be allowed at all, even if closely monitored, the ethical issues indicated in relation to the societal values affected need to be addressed. However, it should be distinguished between cases in which

1. human enhancement is the explicit research goal, and
2. human enhancement is only a likely side-effect or possible application.

Case 1 requires more scrutiny in terms of whether it should be allowed at all, while case 2 requires balancing the (ethical) pros and cons of both the HET-related and non-HET dimension of the proposed project.

While the following is not meant to present an exhaustive or exclusive approach to how ethical issues of human enhancement may be addressed, it may be considered an exemplary way of how to do it. Overall, a three steps approach is suggested:

1. **Identify** HET the *categories*, *domains*, and *societal values* explained above, which fit and are relevant to your research project. Simply make a list of these.
2. **Explain** why and how your research fits the listed HET categories and domains and how the identified societal values are affected. This will help to establish a framework based on which

ethical issues, arising in relation to the identified societal values, can be discussed in a more focused way.

3. **Address** the ethical issues, arising in relation to the societal values affected, and explain how they are supposed to be dealt with. Most importantly, explain how negative implications are supposed to be eliminated or at least alleviated in your proposed project. Indicate how the identified societal values can be safeguarded.

   In addition to the societal values above, also consider the following ethical issues:

   - HET is often prone to **misuse**. Consider the case of cognitive enhancement drugs, which may originally have been developed as medical treatment and now are not only misused for enhancement purposes but also as a lifestyle drug.
   - HET might be **weaponized**. Consider the case of prosthetics, which might allow for military modifications. Or consider cognitive or mood enhancement drugs, which might be used on soldiers to strengthen their combat abilities.

7 Annex 2: Exemplary case studies for illustration

Based on the suggested approach, the following three case studies serve as an exemplary illustration of how ethical issues of HET may be addressed.

7.1 Case study 1: Antidepressants

The (hypothetical) proposed project features research and development on a new antidepressant. Initial research has shown that the new drug can be expected to be more effective in attenuating sudden mood-swings and minimizing phases of severe depression, all of which with fewer and less severe side-effects. Moreover, it is expected that the acclimatization phase is not as long as with previous drugs and effects also wear off faster when one stops taking it. Overall, it is expected that the new drug greatly enhances patients' ability to manage their moods more precisely and effectively. However, it is also more expensive to produce, leading to a substantially higher price than previous drugs.

Initial research has also hinted at the new drug's potential for changes in patients' personality in terms of being more cheerful and sociable, which seems to apply not only to patients suffering from clinical depression but also to healthy persons who could use the drug specifically to induce such enhancing personality effects.

7.1.2. Identify HET categories, domains, societal values affected, and ethical issues arising.

HET categories

- *Affective & emotion*

HET domains

- *Healthcare*

Societal values affected

- *Autonomy*

- *Health & safety*
- *Equality*
- *Fairness*

7.1.3. Explain why and how the identified HET categories, domains, and societal values are affected, and how and why the identified ethical issues arise.

HET categories

Affective & emotion: As an antidepressant, the new drug explicitly aims at affecting patients' affective and emotional states. It deliberately serves as mood enhancement and is also expected to lead to (positive) changes in personality. Consequently, the new drug shows a potential for both therapeutic and non-therapeutic enhancement.

HET domains

Healthcare: The new drug is aimed for clinical use only, which is why primarily the healthcare domain is affected. Yet, the possibility of off-label use or general misuse can never be fully excluded. So, unintentionally, other domains like education, workplace, and home or recreation may be affected as well to some degree.

Societal values affected

Autonomy: As a mood enhancing drug that also brings about personality changes, patients' autonomy may be affected in that it may become unclear in how far decisions and actions are still authentic, which is a central condition of personal autonomy. On the one hand, patients may (maybe for the first time) experience to be really themselves when taking the drug. Accordingly, it is the clinical depression that had undermined their authenticity and autonomy before. On the other hand, patients may experience a sense of alienation and loss of self when taking the drug, putting into question the drug's positive effects, at least when it comes to patients' authenticity and autonomy.

Equality and Fairness: Given the high costs of production and the substantially higher retail price, questions of access to the drug arise. Assuming that not everyone or every health insurance is capable or willing to afford it, the new drug will lead to an unequal and likely unfair distribution. It likely cannot be ensured that everyone who has a medical need for it will actually get it.

Health & safety: As an antidepressant in a clinical setting, the new drug obviously has a bearing on health & safety. Given the promising results of initial research, the expected overall effects can be considered positive, i.e. neither health nor safety will likely be affected negatively.

Ethical issues

Costs: As mentioned above, the high costs of production and the substantially higher retail price, leading to questions of equality and fairness when it comes to access to the new drug, present an ethical issue. Moreover, the high costs also lead to a more general ethical question about the allocation of resource within and to the health care system. Hence, the substantially higher costs in comparison to previous antidepressants need to be justified.

Risks & side-effects: In addition to the costs involved, one of the first ethical questions is usually concerned with risks and possible negative side-effects of new pharmaceutical developments. These

need to be weighed against the expected benefits as well as the costs involved. From an ethical standpoint, research and development of the new drug, therefore, needs to be justified against the background of already existing and effective drugs. Moreover, patients suffering from clinical depression need to be distinguished from healthy persons, as the results of the risk-benefit-analysis may differ—although it needs to be stressed that the new drug is intended strictly for clinical use only.

Misuse: As with all pharmaceutical means, misuse is possible, which raises the ethical question of how this potential for misuse may be considered acceptable and how it can be minimized.

May put into question what counts as normal: If there is a more widespread use, the potential for both therapeutic and non-therapeutic enhancement—albeit the latter only in the sense of unintended off-label use—may lead to a social shift in how people are seen. Instead of seeing people as just being in a melancholy mood but otherwise perfectly normal and healthy, this view might shift and people in such a mood might be more and more considered as requiring medical attention, i.e. as *not* being normal or healthy. Social expectations of how one *should* feel may shift accordingly, maybe even delegitimizing a melancholy mood outright. This raises ethical concerns about a possible delegitimization of what is still and with good reason considered perfectly normal.

May challenge our views of what it means to be autonomous and authentic: Following such a possible shift in the evaluation and normative expectation of how people should be, people who are merely in a bad or melancholy mood may no longer be considered authentic and autonomous. For, both authenticity and autonomy imply standards of normalcy. Accordingly, moods or personality traits now considered abnormal may very well lead to questioning any kind of decision or action as being abnormal and, thus, non-authentic and non-autonomous as well. This raises an ethical concern about how respect for people's autonomy can be maintained under such circumstances.

May lead to a medicalization of characteristics previously seen as normal: Moreover, the above-mentioned shift in social evaluation and expectations may give rise to the idea that certain moods or personality traits that so far have been considered perfectly normal and healthy may then be seen as in need of being medicalized in order to be restored to normalcy. This raises concerns about an ethically illegitimate over-medicalization of traits that should be considered perfectly normal and healthy.

7.1.4. Address the ethical issues and explain how they are supposed to be dealt with.

Costs and Risks & side-effects: The expected substantially higher costs for the new drug may be considered ethically justified when considering the substantially lower risks and negative side-effects, which initial research has shown for the new drug. Hence, the overall cost-risk-benefit-analysis speaks in favor of pursuing research & development of this new drug. This holds both for the perspective of patients who can benefit substantially from this new drug in comparison to existing ones and for the perspective of resource allocation in the healthcare system, which would substantially benefit from the expected better and more effective treatment and results.

Misuse: Although misuse can never be fully eliminated, the usual strict control of access to prescription drugs may be considered as ethically acceptable and effective as with similar drugs.

May put into question what counts as normal: Given that the new drug is supposed to be used in a clinical setting only and access to it is supposed to be appropriately limited, larger societal effects such as described above should not occur. Hence, the proposed research & development and use of the new drug will not give rise to his ethical concern about widespread non-therapeutic enhancement. Moreover, even granting the potential of therapeutic enhancement, the enhancing effects can be closely monitored and limited within a clinical setting.

May challenge our views of what it means to be autonomous and authentic: This ethical concern about more widespread social effects can likewise be considered as essentially irrelevant due to the strict clinical setting of the new drug's use. However, patients' authenticity and autonomy might very well be affected which has implications for the legitimacy of their informed consent. Assuming affective, emotional, and personality changes, it may be doubtful under which conditions an informed consent may be considered legitimate: should only the informed consent given prior to taking the new drug count as legitimate or (also) the informed consent given (or withdrawn) after taking it? This ethical concern is intended to be addressed by making these changes continuously transparent to research subjects and patients and by continuously having consultations and short-term renewals of informed consent under both conditions.

May lead to a medicalization of characteristics previously seen as normal: This ethical concern about more widespread social effects can once again be considered as essentially irrelevant due to the strict clinical setting of the new drug's use.

7.2 Case study 2: Treating dementia

The (hypothetical) proposed project features research & development on a new treatment for dementia. The treatment consists of pharmaceutics in combination with non-invasive brain stimulation. Initial research has shown that the new treatment is effective not only in restoring patients' cognitive abilities, like memory and logical thinking, to a normal level in early stages of dementia but also in enhancing them. Initial test subjects reported that they never felt more cognitively capable.

Based on these early findings, the (hypothetical) proposed project not only aims at further developing treatment options but also a reasonably affordable opportunity for healthy persons to enhance their cognitive abilities. It is expected that the project will lie the groundwork for a huge market of cognitive enhancement.

7.2.1. Identify HET categories, domains, societal values affected, and ethical issues arising.

HET categories

- *Cognitive*

HET domains

- *Healthcare*
- *Education*
- *Workplace*
- *Home or recreation*

Societal values affected

- *Autonomy*
- *Equality*
- *Fairness*
- *Health & safety*
- *Solidarity*

7.2.2. Explain why and how the identified HET categories, domains, and societal values are affected, and how and why the identified ethical issues arise.

HET categories

Cognitive: The proposed treatment explicitly aims not only at restoring cognitive abilities of patients to a normal level but also enhancing cognitive abilities, both for patients and healthy persons. Consequently, the proposed treatment includes both therapeutic and non-therapeutic enhancement.

HET domains

Healthcare: In terms of restoring and enhancing cognitive abilities of patients, the proposed project is situated in the healthcare domain.

Education, Workplace, Home or recreation: In terms of enhancing cognitive abilities of healthy person, the proposed project goes beyond the healthcare domain and a substantial impact may be expected in the following domains: education, workplace, and home or recreation.

Societal values affected

Autonomy: Autonomy would be affected in a twofold way. On the one hand, since cognitive abilities play an important role in our capacity of being autonomous, enhanced cognitive abilities would allow for improved reflection skills and, thus, promote autonomy. On the other hand, autonomy in the sense of being able to realize one's authentic desires and preferences in society would likely be diminished. Assuming a widespread availability and attractiveness of the proposed treatment, a lot of people would likely make use of it, not the least in order to enjoy its advantages in education, workplace, or in private life. This would likely lead to an increase in competition and social pressure to use the treatment, or else falling behind. Hence, the option not to use cognitive enhancement would in comparison become less and less attractive, which, in turn, would diminish the autonomy of those who would prefer this option.

Equality: Assuming that not everyone would be eager to use the treatment, but that those who do would gain significant cognitive advantages over non-enhanced persons, this would lead to an increase in inequality in society.

Fairness: Assuming that there would be an increase in social inequality, that enhanced people would enjoy cognitive advantages over non-enhanced people, and that not everyone would have equal access to the treatment, this would likely put the value of fairness into jeopardy whenever enhanced people would compete with non-enhanced people.

Health & safety: The treatment itself will likely involve some minor health risks, which usually come with pharmaceutics. Yet, overall, it can be considered reasonably safe, also due to the brain stimulation being non-invasive.

Solidarity: Assuming that the treatment would be widely available, there could be a decline in solidarity in society with those people who do not want to use the treatment. This holds especially in case non-enhanced people would face a situation with a negative impact that could have been avoided had they used the treatment.

7.2.3. Ethical issues

Risks & side-effects: Although the proposed treatment can be considered reasonable safe and free from negative side-effects, some remaining risks will be unavoidable. This raises an ethical concern of how to deal with it and limit possible risks and negative side-effects.

Social coercion to use HETs & a HET "arms race" and an increase in social competition: Assuming that cognitively enhanced people would enjoy additional advantages over non-enhanced people and that this would lead to an increased social pressure to use the treatment as well, this could very well lead to an ethically dubious increase in social competition and to an "arms race" in striving for ever more effective and powerful cognitive enhancements in order to stay on top.

May challenge and put into questions societal values, such as equality, fairness, and solidarity: A widespread availability of the proposed treatment would likely affect well-established societal and ethical values, especially equality, fairness, and solidarity, as described above.

May put into question what counts as normal: A widespread availability of the proposed treatment would likely lead to a shift in what level of cognitive capacity is considered normal. The more people will enhance their cognitive abilities, the more this enhanced level will be taken for granted and thus expected of everyone.

May lead to a medicalization of characteristics previously seen as normal: Assuming such a shift in normative expectations of which level of cognitive capacity is considered normal, any non-enhanced capacity, which by definition falls short of the new higher level, would likely be seen as defective and in need of medicalization.

7.2.4. Address the ethical issues and explain how they are supposed to be dealt with.

Risks & side-effects: As mentioned above, the proposed treatment will inevitably involve a potential for risks and unintended side-effects. Yet, initial research has shown that both are likely not severe and limited in their scope. Hence, the corresponding ethical concern is not drastically different from already available treatments and other means of cognitive enhancement. The proposed project, thus, does not lead to any special ethical issue in this regard.

Social coercion to use HETs & a HET "arms race" and an increase in social competition: In light of the value of individual liberty and allowing people to decide for themselves if they want to make use of the treatment or not, the possible result of an increase in social pressure to use the treatment cannot be fully avoided, just like with a lot of other means to gain social advantages. Hence, the tension

between promoting individual liberty and limiting its unintended social results of a HET "arms race" and an increase in social competition will be impossible to resolve satisfactorily to begin with. Yet, the ethical concern about it can be considered less severe in this case when taking into account that the proposed treatment is aimed to be reasonably affordable and not involving severe risks or negative side-effects.

May challenge and put into questions societal values, such as equality, fairness, and solidarity: Given the likely result of an increase in social inequality due to a division between enhanced and non-enhanced people, it needs to be assessed in how far this could still be considered ethically acceptable, especially in comparison to already available means of cognitive enhancement and gaining social advantages in society. Social inequality is, unfortunately, a matter of fact. The ethical question is thus "merely" if the proposed treatment may further increase it. Given that the project aims at developing a reasonably affordable opportunity for cognitive enhancement, such an increase would at least not be due to financial inequality but could be traced back to people's choice about making use of it or not. Given that the individual liberty to choose is a core value in modern liberal societies, the proposed project would clearly adhere to and promote this value. However, assuming that not everyone will choose to use the treatment, there will be some more social inequality in this regard. This would need to be addressed on a social or political level, which is obviously beyond the scope of the proposed project. Much the same holds for addressing fairness and solidarity. Both values, as described above, would likely be affected. Yet, addressing the ethical concerns that go with them if the proposed treatment is widely available has to be considered a social and political challenge. For instance, steps need to be taken in order to ensure that non-enhanced people still have a fair chance when it comes to job applications or other competitive social practices. Moreover, a political solution is desirable in order to ensure solidarity in society for non-enhanced people. This might, for instance, include the establishment of public insurance or other means of support. From an ethical point of view, this would need to be backed up by public reasons that promote people's right to choose not to get cognitively enhanced and not having to face undue disadvantages when doing so.

May put into question what counts as normal & may lead to a medicalization of characteristics previously seen as normal: In order to address these ethical worries, one needs to distinguish between two meanings of "normal": a purely descriptive, statistical notion and a normative notion which includes social expectations. While a shift based on the first notion is not an ethical problem at all and a simple matter of changed situations and characteristics, the second notion gives rise to an ethical issue if a shift in social expectations leads to undue social pressure to meet these expectations, i.e. to use cognitive enhancement and no longer being autonomous not to do so. Again, this ethical challenge goes way beyond the scope of the proposed treatment and needs to be addressed on a social and political level, preferably again by public debate that promotes people's right to choose not to get cognitively enhanced and not having to face undue disadvantages when doing so. Hence, public and political debate as well as accompanying norms and regulations would need to make clear that there is no "new normal" in the second, normative sense.

7.3 Case study 3: Genetics

Research in the domain of genetics bears lots of potential benefits as well as risks. Despite its widely accepted therapeutic usage, a vast amount of research in this domain could potentially be used for

enhancement purposes. Think of, for example, human genome editing via CRISPR (Clustered Regularly Interspaced Short Palindromic Repeat) that could be used beyond therapeutic goals to enhance certain traits. Similarly, via genome editing in IVF, parents could be tempted to choose specific features for their unborn children with the idea of designing their babies according to their preferences. Given that it is hard to draw a clear-cut line between therapy and therapeutic enhancement, such cases will soon become more pressing. Consider, for instance, the case of the first CRISPR-babies, born in China in November 2018, who have been designed to be immune to AIDS. Should such immunity still be considered therapy or rather therapeutic enhancement?

Were such possibilities be made readily available on a large scale, this would inevitably bear the potential of genetically enhancing not just the occasional individual but entire populations. Genetic engineering that can potentially be used to extend the human lifespan beyond its current natural limitations, might look innocuous at first glance, but such interventions into human nature go beyond merely restoring the natural functioning of human physiology and can as such be seen as enhancement.

Importantly, researchers might not intend their research findings to be used in any of the HET ways mentioned above, but nonetheless once they bear such enhancement potential, they give rise to ethical questions.

Research in genetic engineering is so far-reaching that it could potentially affect all categories, domains and societal values. Moreover, one might argue that not only genetic engineering, but already wide-spread embryo selection could have such far-reaching eugenic effects. In what follows, we focus on a few of them.

7.3.1. Identify HET categories, domains, societal values affected, and ethical issues arising.

HET categories

- physical
- cognitive
- behavioral & affective
- cosmetic
- moral
- longevity

HET domains

- *healthcare*
- *education*
- *workplace*
- *military/defense*
- *home or recreation*

Societal values affected

- *autonomy*
- *dignity*
- *equality*
- *fairness*
- *health & safety*
- *peace*
- *privacy*
- *respect for human life*
- *solidarity*

7.3.2. Explain why and how the identified HET categories, domains, and societal values are affected, and how and why the identified ethical issues arise.

HET categories

Physical: Genome editing interferes with the human organism on its most basic level. The potential consequences of such interventions reach from minor changes in the genetic make-up of a person that prevent or cure certain diseases, to major changes in the person's organism that can influence virtually all physical characteristics. Such interventions could be used to promote certain traits in large populations which bears the potential of permanently altering human nature.

Longevity: One such alteration might affect the currently natural lifespan humans typically have. If genome editing advances to a degree which allows for increasing life expectancy, society might face unheard-of challenges.

HET domains

Healthcare: Since its original purpose was therapeutic, genome editing is initially located in the healthcare domain. However, as aforementioned, its wide ranging potential and possible applications will ultimately affect all the domains of human life.

Societal values affected

Autonomy: Issues of autonomy when genome editing is used for reproductive purposes have an effect on both the well-fare of potential children and the reproductive autonomy of parents. Were parents to be able to pick out features they want for their children, this might increase their autonomy at the cost of increasing parents' responsibility. If the element of chance is removed, parents will be "hyper-responsible" for the fate of their children. This, on the one hand, could benefit children's well-fare (if parents pick the right features), but could also harm children's well-fare (if parents pick the wrong features). Also, if so much is decided by parents on their children's behalf, it is unclear how much autonomy remains that allows children to go make their own choices later in life.

Respect for human life: Among other things, a widespread use of genome editing that goes beyond therapeutic intends has the potential to alter human nature in ways that are difficult to foresee.

Accordingly, tempering with human nature bears potential risks and unintended side effects that can hardly be anticipated, let alone prevented.

7.3.3. Ethical issues

Risks & side effects. Regarding CRISPR's potential to physically alter the human organism, the therapeutic promise as for example in being able to modify pathological genes must be weighed against potential risks. Apart from the well-known medical risks of gene editing technologies that could potentially lead to serious harm to research participants, currently the long-term effects of such interventions remain largely unknown.

Moral status. Experiments on human embryos, for example, are both morally and legally controversial. Moral issues include questions regarding the embryo's moral status which might imply a right of non-interference. Were embryos seen as persons, researchers would then be morally obligated to grant them a right of life.

Privacy. Altering human genomes poses potential risks for privacy and confidentiality breaches, as information so collected might become available for unintended use. This is not a problem inherent to research in genetics, but because of the sensitivity of the collected information requires extra caution.

Eugenics. Were large populations to alter human genomes with the intention to make themselves or their offspring fit better in society, this might in turn lead to societal demands that require what was previously not required of humans due to their genetic limitations. Such population-wide promotion of certain traits, resembles eugenic practices of the past, and severely impacts diversity and freedom in that it asks of us to tailor ourselves to what society demands, instead of creating a society that accommodates human nature. Needless to say, such eugenics could not simply reflect societal demands but also have ideological agendas.

Misuse. Besides eugenics in general as one potential misuse, it is also possible that particular institutions such as military facilities might have an interest in promoting the use of genome editing to alter the genetic make-up of, say, soldiers in a way that reflects such institution's particular needs. Such alterations could result in a conflict of interest between what features military facilities might their soldiers want to have (say ruthlessness or lack of empathy), and what these people themselves want to be.

7.3.4. Address the ethical issues and explain how they are supposed to be dealt with.

Risks & Side effects. Since the potential risks and side-effects of genome editing that is comparatively in its infancy is very difficult to anticipate, each new application of genome editing must be accompanied by a thorough ethically-informed technology assessment. Precisely because potential applications are far-reaching, a case-by-case assessment of its potential risks and side-effects is vital. Since there are potential conflicts of interests between research, application, and society in general, it appears necessary to have an institutionalized independent ethical review process.

Moral status. The contentious issue of moral status of embryos is not new and has been dealt with particularly in the debate on abortion. Since, however, genome editing is not a matter of life and

death in most cases, it might raise new questions regarding mild interference. It seems as though as long as the purposes of interference remain therapeutic, there should be little to no ethical concern. Once the threshold to enhancement is crossed, however, the issue becomes much more contentious. Here one would need to address questions as to the purpose of the striven for enhancement and its potential long-term consequences both for individuals and society.

Privacy. The issue of potential privacy violations of sensitive data requires extra caution since genomic information is particularly sensitive and could be used for all sorts of harmful purposes by third parties. Therefore, such information must be stored very securely. New protocols and security measures that are tailored towards storing genomic information must be maintained.

Eugenics. The potential of genome editing being used for eugenic purposes, either on an individual basis as liberal eugenics or in terms of a state-driven eugenics program, is a serious threat that must be taken into consideration whenever an application is developed that bear even a remote potential for being used that way. It is, therefore, vital to have an ethical oversight in place in all stages of development and application of such technologies. In particular, it will be necessary to make sure that no societal pressure undercuts autonomous choices of individual people. Therefore, it seems imperative to make sure that genomic editing is not used on a large-scale societal level with the sole purpose of promoting certain features that aim at altering human nature beyond restoring health.

Misuse. A potential misuse can never be fully excluded. However, in the case of institutionalized application of genome editing, the potential threat of such misuse is imminent. This is why where such institutionalized use is necessary, it is imperative to have in place a continuous, independent ethical assessment that weighs potential benefits and risks for individuals, and critically reflects on (hidden) institutional agendas.